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Where Are Drugs Invented, and Why Does It Matter?

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ABSTRACT: Globalization has disrupted many industries, initially shifting unskilled labor employment from high wage-cost industrialized nations to lower wage-cost emerging economies. There has been a trend toward moving increasingly skilled work away from industrialized nations, which raises the question—has innovative research and development been affected by globalization, and why is relocation of innovation much more than a simple economic concern?

According to the biotechnology innovation organization, biotechnology can "Heal, Fuel, and Feed the World." But leadership in biotechnology and biomedical innovation can provide benefits beyond useful products for health and industry. Leadership in biomedical domains can extend to improved quality of life for citizens, and the improvements in economic productivity and global political status that improvements can bring.

A prominent and oft-cited example of the global political and economic impact of biomedical innovation is the construction of the Panama Canal. The concept of the Panama Canal traces back to the 1500s when Spain's King Charles V sought a shorter route for ships traveling between Spain and Peru, with the objective of providing the Spanish a military advantage over the Portuguese. As a testament to the challenge of building the canal, French efforts to build the canal in the 1800s were abandoned after an estimated 22,000 workers died of diseases such as Malaria and Yellow Fever. By instituting innovations in public health the United States was ultimately able to successfully construct the canal with much lower attrition than French efforts.[1]

Just as the US today enjoys many economic and political benefits from the Panama Canal, it also enjoys great benefits from rapid growth in scientific output surrounding and after the Second World War. Today the US has the world's largest economy, and it also spends more on research and development than any other country (for many years the US accounted for more R&D spending than the rest of the world, combined).

CAN INDUSTRIALIZED ECONOMIES CONTINUE TO ENJOY THE BENEFITS OF GLOBAL INNOVATION?

There are two direct benefits that stem from the aforementioned US leadership. First, with a large economy, enterprises in many other countries (especially in small ones) will aim to target the US market for their goods and services. Second, with a strong R&D base, US policymakers can direct national assets to addressing domestic needs (e.g., the Space Race, the War on Cancer, etc.). These benefits mean that large economies with strong research and commercial bases can be favorably positioned to obtain the innovative products and services they need.

As numerous economies, which were once categorized as developing, increase their economic base and R&D output, and as some industrialized economies demonstrate decreased R&D spending or stagflation, an important question emerges—will the attention of innovators shift away from the established economies?

For example, in 2010 China surpassed the United States in the estimated number of researchers.[2] In 2015 the estimated purchasing power parity adjusted gross expenditure on research and development (GERD) for the United States was US $503bn, China's GERD was US$409bn, and the European Union's GERD was US$384bn. Further, while the US and EU GERD increased ∼20% from 2010 to 2015, China's GERD increased by more than 90%.[2] So it seems likely that China's GERD will expand its lead over the EU, and potentially catch up with the US.

Currently some of the most popular therapeutic indications for drugs in development are diseases prevalent in Western countries, such as diabetes, breast cancer, leukemia, etc.[3] If attention in drug development were to shift to diseases less prevalent in Western countries, such as liver disease and stomach cancer, then treatments for Western diseases could become more expensive, or simply unavailable.

IMPLICATIONS FOR DRUG DEVELOPMENT

Given growth in GDP and in R&D spending in countries such as China, it is desirable to assess the impact of their research efforts.

The US Food and Drug Administration's (FDA) procedure for approving generic pharmaceutical drugs provides an excellent objective foundation to measure global performance in drug development. To control generic entry, developers of innovative drugs are required to submit to the FDA all the patents protecting their drugs. The objective listing of patents for drugs can be used to study inventor locations because the US Patent and Trademark Office has firm rules specifying that the US patents must include *all* the individuals who had "intellectual domination" of the invention.[4] Listing too few or too many patents can yield an unenforceable or invalid patent. Further, US patents list the locations of each inventor.

So, US patents can be used to objectively identify the locations of pharmaceutical drug inventors for drugs approved and patented in the US. Because the US is the world's largest drug market, and US patents are required to protect drug intellectual property in the US, this linkage can be used to

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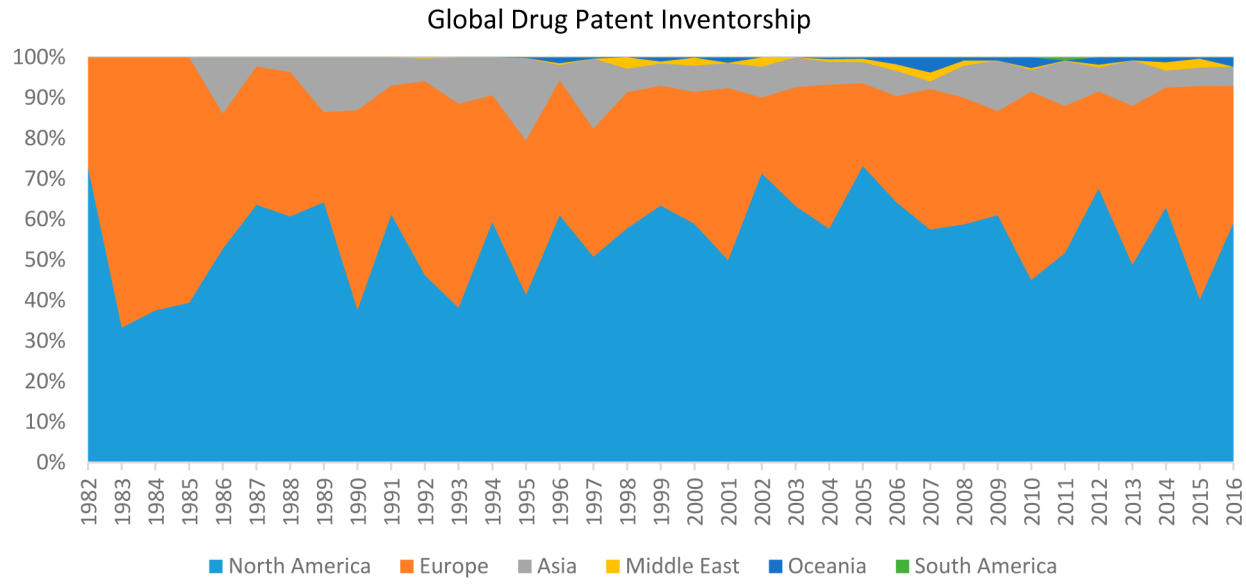

Figure 1. Global drug patent inventorship.

Table 1. Asian Drug Patent Inventorship

country	1982−1986	1987−1991	1992−1996	1997−2001	2002−2006	2007−2011	2012−2016
Japan	5	24.3	71.3	122.1	99.6	119.8	102.6
South Korea	0	0	0	0	4	0	4.4
China	0	0	0.3	0	3.3	2.2	2.2
India	0	0	0	0	0.8	2.8	4
Taiwan	0	0	0	0	0	0.3	1
Brunei	0	0	0.3	0.3	0	0	0

identify inventor locations, albeit with a potential US-centric bias. Using a technique similar to a prior study,[5,6] historical drug approval and patent information was obtained from the DrugPatentWatch.com platform[7] to examine trends in the locations of drug patent inventors.

An annual regional perspective on drug patent inventor locations is shown in Figure 1. North America (largely the United States) accounts for more than half of the drug patent inventorship, European nations account for one-third of the inventors, and Asian countries account for just over 7%. An immediate observation is that there are no apparent gross trends in expansion of Asian participation nor lower participation of European or North American countries. Inventors in Oceania (entirely represented by Australia here) and the Middle East (largely Israel here) have visible participation starting in the late 1990s, suggesting a possible contribution of the emergence of the World Wide Web in facilitating international collaborations.

A closer examination of the patent-producing Asian countries demonstrates little contribution from the emerging economies. Table 1 shows a focus on inventors in Asian countries. The immediately apparent result is that Japanese inventors represent nearly all the Asian drug patent inventors. In recent years Japan's dominance of Asian inventorship has slipped from >99% to just under 90%. The countries filling this gap are South Korea (3.9%), India (3.5%), China (1.9%), and Taiwan (0.9%).

CONCLUSION

In the years since this methodology was first deployed,[5] a familiar response was to "just wait a few years" to see the results of increased R&D investments in emerging economies. The results from the forward- and backward-expanded analysis presented here suggest that it may be decades before substantial contributions in drug inventorship come from countries that are not currently represented. Consider that Australia and Israel, which have seen strong economic and R&D growth since the late 1990s, are still relatively minor contributors to global drug invention. This suggests that even if a country like South Korea or China were to dedicate substantial resources to novel drug development, there is still a long incubation period, and potentially also a minimum output threshold to overcome, before significant domestic drug development efforts can bear fruit.

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Notes

The author declares the following competing financial interest(s): I am the owner and publisher of DrugPatentWatch.com.

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(2) OECD Main Science and Technology Indicators Database, February 2017.

(3) Analysis of clinicaltrials.gov data from January 2012−December 2016, data not shown.

(4) Morse v. Porter, 155 USPQ 280, 283 (Bd. Pat. Inter. 1965).

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(6) Briefly, the set of drugs receiving US approval in 1982 or later was examined. For each drug the patents, which were filed prior to drug approval, were included in the study in an attempt to exclude late-filed patents that might protect novel formulations, salts, etc. Each patent was counted on par, with the inventor's countries being weighted according to their representation. For example, for a patent with a single German inventor, Germany would get credit for one patent. For a patent with two Canadian and one United States inventors, Canada would get 2/3 credit for a patent, and the United States would get 1/3 credit. These relative inventorship scores were then compared against the annual total number of patents to determine the contribution of each country's inventors to that year's pool of drug patents.
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